REFERENCES

1. Guyatt GH, Sackett DL, Adachi JD, et al: A clinician's guide for conducting randomized trials in individual patients. Can Med Assoc J 1988; 139:497-503

2. Jaeschke R, Guyatt G, Keller J, et al: Ascertaining the meaning of a change in quality-of-life questionnaire score: Data from N of 1 randomized trials. Controlled Clin Trials, in press

3. Guyatt GH, Keller JL, Jaeschke R, et al: Clinical usefulness of N of 1 randomized control trials: Three year experience. Ann Intern Med, in press

Are Vitamin A Supplements Needed During Pregnancy?

THE INTRODUCTION of therapeutic retinoids in the 1980s for the treatment of severe acne and psoriasis led to initial claims that these were "miracle" drugs. Within several years of their approval for marketing, however, it became clear that these retinoids posed an unusually high risk for adverse outcomes of pregnancy when taken after conception. The unusual magnitude of this teratogenic risk, coupled with the fact that vitamin A (retinol) was known to induce identical malformations in an experimental setting, has prompted reasonable concerns that supplementation with retinol during pregnancy may be hazardous to developing embryos and fetuses.

This concern will be heightened if experimental studies find that the teratogenic properties of retinol are largely mediated by its metabolic conversion to retinoic acid. This has not been conclusively demonstrated yet, and it is unclear whether retinol induces malformations independently.[1] There are several important pharmacokinetic differences between retinol and retinoic acid that probably act to reduce the potential for human retinol teratogenicity.[2] First, the intake of retinol, in contrast to that of retinoic acid, is necessary for human health, and so a sophisticated system has evolved to maintain body storage and to regulate the serum concentration available to other tissues. Retinol is stored in liver cells and is bound in serum by a specific carrier protein, retinol-binding protein. Excess absorbed retinol is rapidly removed from the serum and stored. Retinoic acid, on the other hand, is not stored and is nonspecifically bound to serum albumin. These different properties make it less likely that excess vitamin A intake might be teratogenic compared with retinoic acid. It is unknown whether excess retinol intake might substantially increase serum levels of all-*trans*-retinoic acid.

Although concerns about the possible teratogenicity of vitamin A are reasonable, there are no systematically conducted human studies to quantitate this risk. Werler recently found a twofold increased risk for vitamin A supplementation and malformation of structures that are composed, at least in part, from cranial neural crest cells.[3] This cell population has been shown to be susceptible to retinoic acid exposure in utero. Werler's study found that 0.2% of control mothers took a vitamin A supplement during early pregnancy. Other surveys have shown geographic variations in vitamin A supplementation but generally have found that less than 0.5% of nonpregnant women of reproductive age take vitamin A supplements of 25,000 IU per day or more. Given this low frequency of supplementation, it will be difficult to identify small increased risks for major malformations in human studies.

The recommendations of Kizer and associates and the Teratology Society to limit the maximum amount of vitamin A per unit dose are sensible and should be implemented. I do not agree that an increased need has been found for vitamin A during pregnancy that requires supplementation. Like most of the components of vitamin supplements taken during pregnancy, vitamin A has traditionally been included in the supplement without any evidence that the usual dietary intake is inadequate and without any evidence that supplementation in developed countries is beneficial to mother or fetus. In developed countries, there appears to be little or no scientific basis for supplementing pregnant women with retinol or retinyl esters, while there is a small possibility of causing harm. It makes sense that vitamin supplements taken prenatally, if they contain vitamin A at all, ought to include only β-carotene as the source of vitamin A. An argument can easily be made that this logic holds for using β-carotene as the source of vitamin A for all commercially available supplements. Regulatory agencies should work with manufacturers to bring about such changes.

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REFERENCES

1. Eckhoff C, Nau H: A Possible Role of All-*trans*-Retinoic Acid as an Active Mediator of the Teratogenicity of Vitamin A (Abstr). 17th Conference of the European Teratology Society, Budapest, September 4-7, 1989

2. Teratology Society: Recommendations for vitamin A use during pregnancy. Teratology 1987; 35:269-275

3. Werler M: Maternal Exposures in Relation to Birth Defects. PhD thesis. Boston, School of Public Health, Boston University, 1989

Health Care—Where Are the Problems and Where Are the Solutions?

THE BASIC PROBLEMS in what we call health care are problems for the patient, the family, and, to a greater or lesser extent, the immediate health care environment of an ill person. The problems are actually problems of illness rather than of health, and the first and most important steps in health care have to be taken where the sick, injured, or emotionally disturbed person is, with the resources for care that are available. This is what health care is all about. Yet there are many who view it differently. They see it more as a national problem that, therefore, requires a national solution, by which they mean a nationalized system for rendering patient care. This view is reinforced by the rising cost of health care, which is now nationwide and has become a problem not only for the persons afflicted, their families, and the immediate community, but for business and industry and even for government at the local, state, and national levels. For some time we as a nation have been wont to turn to government when things need to be done that are beyond the reach of individuals or local communities. Government can spread the costs over a wider base, and this substantially reduces personal responsibility for them. The pain of the cost is softened until tax time, and even then it is more often directed toward the amount of the tax, with little consideration of the value of the benefits that in most cases seem to accrue to someone else.

But the fact is the problems of health care and its costs affect almost everyone. They can be viewed as personal, community, local, state, and national problems. For a while there was considerable enthusiasm for a comprehensive, all inclusive program of national health insurance to be administered and paid for by government. As costs have risen, enthusiasm for this has cooled. Actually, a trend quite the opposite has begun to develop. Among the myriads of health care plans and programs that have come into being in business and industry and in government at all levels, there is a notable tendency to push responsibility for paying the costs down-

ward. There is evidence that federal programs are unloading more of their costs onto the states, and, in California at least, the state has started to shift more of the burden down to the counties. The private sector, in similar fashion, has begun to make the beneficiaries participate more directly in the cost of the benefits. This growing decentralization of responsibility and payment for health care costs causes community and personal fiscal pain. It may result in a renewed demand for greater centralization of health care, notwithstanding the evidence that when bureaucratic efforts to control costs are successful, they are done insensitively and at the expense of needed care.

This trend toward decentralization in the long run may be a good thing, however. It could be that the present day problems of health care can be better solved from the bottom up, relying more on local sensitivity and control, rather than depending too much on decisions and choices that are made remote from the real problems of patient care. It would seem more reasonable to look for solutions at the local and perhaps regional level. Americans are pretty good at solving their own problems when they recognize a need. They can be truly innovative in developing available resources to meet their perceived needs. Dollars are part of the problem in health care. Perhaps it is time for health care dollars, collected in taxes and insurance premiums, to flow more freely to where the needs and problems of access, quality, and cost of care are the real, everyday problems of those directly concerned, giving local options more of a chance.

In this connection, we should not forget that no matter how health care is managed or where it is managed, there will never be enough dollars—the demands and expectations will always exceed what can be done with the available resources. Somewhere, hard choices have to be made. It would seem that this could be done more fairly at the local level. Someone has pointed out that there is precedent for Americans making hard choices at the local level. In earlier times this occurred at town meetings. More recently, during World War II, local boards administered a draft law where hard choices had to be made about who would have to offer his life for family, community, and country. This was done by a lottery, with review by a local draft board. There was reasonable fairness. Perhaps something like a health care number and a local health care board could be developed as a means to help make some of the hard decisions fairly and at the local level as to who is to get what in the way of expensive care that is needed but is beyond the basic services that can be afforded for everyone. The inescapable fact remains: the most important and fundamental problems in health care are the problems of providing care at the local level. It is here where the national solutions ought to be found, and it is here where the American system, given a chance, can be at its best.

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